# Approvals, FDA Actions, Clinical Trials

## FDA ACTIONS

Marketing can resume for Biogen Idec's **natalizumab (Tysabri)** under a detailed, restricted distribution program. The U.S. Food and Drug Administration approved Biogen's risk management program to minimize the potential for progressive multifocal leukoencephalopathy in patients taking natalizumab, which is indicated only as monotherapy. Analysts think natalizumab still could become a blockbuster in a market with widespread unmet need, but achieving that status will take years of slow and steady growth.

The FDA approved orphan drug status for SciClone Pharmaceuticals' **thymalfasin injection (Zadaxin)** for malignant melanoma; to the Netherlands' Pharming Group for its **recombinant human C1 inhibitor** in the treatment of delayed graft function; and to Isis Pharmaceuticals' **ISIS 301012,** a second-generation antisense drug in the treatment of homozygous familial hypercholesterolemia. ISIS 301012 inhibits apoB-100, a key protein in the synthesis and transport of LDL and VLDL cholesterol.

Neurocrine Biosciences received a not-approval letter for its 15 milligram tablet for **indiplon,** a sleep aid, but its 5- and 10 milligram doses were deemed approvable by the FDA pending reanalysis of clinical trial data. … The FDA also sent an approvable letter to Cephalon for **armodafinil (Nuvugil),** an antinarcolepsy therapy.

The FDA granted fast track designation for Caprion Pharmaceuticals' **Shigamabs** for the treatment of shigatoxin-producing bacterial infections. No therapies exist for hemolytic uremic syndrome, which may result in these infections. The agency also fast-tracked TargeGen's cardiovascular compound, **TG100-115,** for the treatment of acute ST-elevation myocardial infarction, and Nektar's **Amphotericin B** inhalation powder, a lung-infection-prevention drug.

Genentech filed a supplemental Biologics License Application for **bevacizumab (Avastin)** as frontline therapy for breast cancer. The FDA, meanwhile, accepted Centocor's sBLA for **infliximab (Remicade)** for inhibition of structural damage and improving physical function in patients with psoriatic arthritis.

## CLINICAL TRIALS/ DRUG DEVELOPMENT

In a phase 3 study presented at the American Society of Clinical Oncology, Pfizer's **sunitinib (Sutent),** already approved for kidney cancer, almost doubled progression-free survival time in patients with advanced clear-cell carcinoma kidney cancer, compared to standard interferon-alpha treatment. Sunitinib also shrunk non-small cell lung cancer tumors and stopped their growth in patients who had received prior treatments.

Other developments from ASCO: In combination with standard chemotherapies, **bevacizumab** extends survival time without disease progression in patients with advanced colorectal cancer. … Genzyme's **alemtuzumab (Campath)** showed higher overall and complete response rates than GSK's chlorambucil (Leukeran) in previously untreated patients with progressive B-cell chronic lymphocytic leukemia. … Amgen's **panitumumab,** which recently received priority-review status from the FDA, shrunk tumors in 13 percent of patients with metastatic colorectal cancer whose tumors did not respond to standard chemotherapy, and stopped tumor growth in 30 percent. … Celgene's **thalidomide (Thalomid),** in combination with dexamethasone, led to a statistically significant improvement in median time to disease progression, the primary endpoint, in patients with multiple myeloma.

At the 2006 European Congress of Rheumatology (EULAR), researchers presented data showing that the benefits of **abatacept (Orencia)** are sustained up to 18 months in patients who have rheumatoid arthritis. The data were part of a one-year, open-label extension of the ATTAIN trial, which focuses on patients with inadequate response to anti-TNF therapies.

The FDA halted a phase 3 trial of Threshold Pharmaceuticals' enlarged-prostate drug **TH-070** because of abnormal liver enzymes in three participants. A phase 2 trial will continue while the FDA requests more information. … **ALS-02,** Avicena Group's drug for Lou Gehrig's disease, failed to show a benefit compared to placebo in a phase 3 trial, but did show decreased mortality in those who took ALS-02. Researchers will examine the results to help Avicena determine whether this finding will affect the drug's regulatory path.

In several phase 2 trials of note, Millennium Pharmaceuticals' **MLN-**

## SELECTED FDA BIOLOGIC DRUG APPROVALS, MAY–JUNE 2006

| Action date | Drug name (Trade name) | Sponsor | Indication | Dosage form | Strength |
|---|---|---|---|---|---|
| *New drug approvals* | | | | | |
| May 2, 2006 | Decitabine **(Dacogen)** | Pharma-chemie BV | Myelodysplastic syndromes (MDS) | Injection; Intravenous | 50 mg/vial |
| May 30, 2006 | Somatropin [rDNA origin] **(Omnitrope)** | Sandoz | • Long-term treatment of pediatric patients who have growth failure due to an inadequate secretion of endogenous growth hormone<br>• Long-term replacement therapy in adults with growth hormone deficiency | Injection | 5.8 mg/vial<br>1.5 mg/vial |
| June 28, 2006 | Dasatinib **(Sprycel)** | Bristol-Myers Squibb | Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast-phase chronic myeloid leukemia with resistance or intolerance to prior therapy, including imatinib **(Gleevec)** | Tablet | 20 mg<br>50 mg<br>70 mg |
| *New and expanded indications* | | | | | |
| May 25, 2006 | Thalomid **(Thalidomide)** | Celgene | Newly diagnosed multiple myeloma, in combination with dexamethasone | Capsule | 50 mg<br>100 mg<br>200 mg |
| *Biologics license approvals* | | | | | |
| June 30, 2006 | Ranibizumab **(Lucentis)** | Genentech | Neovascular (wet) age-related macular degeneration | Injection | 0.05 mL |
| *Supplemental biologics license approvals* | | | | | |
| May 9, 2006 | Antihemophilic Factor VIII [recombinant] infusion **(Advate)** | Baxter Healthcare | Prevention and control of bleeding; management of perioperative bleeding in patients with hemophilia A | Intravenous | Ultra-high (5 mL) |
| May 19, 2006 | Infliximab **(Remicade)** | Centocor | Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderate to severe Crohn's disease with inadequate response to conventional therapy | Intravenous | 100 mg/vial |
| June 20, 2006 | Bevacizumab **(Avastin)** | Genentech | Adjunct to 5-FU-based chemotherapy for second-line treatment of patients with metastatic colorectal cancer | Intravenous infusion | 100 mg/vial<br>400 mg/vial |

5-FU=5-fluorouracil.
SOURCES: FDA, MANUFACTURERS' PACKAGE INSERTS

**1202,** a novel humanized monoclonal antibody, met its primary endpoint. MLN1202, which targets the CCR2 chemokine receptor, reduced the levels of C-reactive protein in patients at risk of atherosclerotic cardiovascular disease. … OSI Pharmaceuticals' **pegaptanib (Macugen)** maintained or improved vision in 90 percent of patients with central retinal-vein occlusion, compared to 69 percent who received a placebo. … Two studies of Amgen's **denosumab** showed rapid suppression of bone turnover in advanced cancer patients with bone metastases.

## MISCELLANEOUS

A meta-analysis of nine trials reveals an increased risk of gastrointestinal, breast, and lung malignancies and serious infections in RA patients with treated for 3 to 12 months with anti-TNF therapies **infliximab** and **adalimumab (Humira).** The analysis was published in the May 17 issue of *JAMA*. The *Chicago Tribune* quoted the manufacturers as saying the risks are not new and have been included in product labeling for years.

— *Bob Carlson, MHA*